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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,517	12/06/1999	BRADFORD J DUFT	235/013US	1018

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Intellectual Property Department
Amylin Pharmaceuticals, Inc.
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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/445,517	DUFT ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-29,31-39,68-80,82 and 84-97* is/are pending in the application.

4a) Of the above claim(s) *25, 26, 28, 35, 36, 69-71, 73-75, 77-79 and 85-94* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,27,29,31-34,37-39,68,72,76,80,82,84 and 95-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *031210*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicant's submission filed on 03/12/10 has been entered.

Applicants' Response

2) Acknowledgment is made of Applicants' response filed 03/12/10 in response to the Advisory Action mailed 05/28/08.

Status of Claims

3) No claims have been amended or canceled.

Claims 23-29, 31-39, 68-80, 82 and 84-97 are pending.

Claims 23, 24, 27, 29, 31-34, 37-39, 68, 72, 76, 80, 82, 84 and 95-97 are under examination.

Information Disclosure Statement

4) Acknowledgment is made of Applicants' information disclosure statement filed 03/12/10. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Prior Citation of Title 35 Sections

5) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

6) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Response to Applicants' Arguments

7) Applicants submit Exhibit 1 and the following arguments.

The specific rejections to which the evidence and the arguments are applicable are stated as those that are set forth at sections 21 and 22 of the Final Office Action asserting double patenting, and sections 25, 26, 27, 28 and 29 asserting anticipation. Applicants' Exhibit I apparently demonstrates that weight loss was not observed in all patients who had diabetes and in many cases were also obese, that were administered pramlintide specifically to treat their diabetes by controlling their blood sugar. Applicants state that as indicated in page 1 of Exhibit I, pramlintide was administered at 120 micrograms twice a day to patients with diabetes and *who were also taking insulin* (Group A). The results at pages 3-4 of Exhibit I are stated as showing the proportion of patients that did not gain weight (either *lost weight* or were weight neutral) with pramlintide treatment (i.e., Group A) to be 46.4%, indicating that 53.6% did gain weight. Applicants submit that a patient treated for control of blood sugar according to the cited art would not have necessarily and inevitably also achieved weight loss. Applicants state that the evidence provides support for their previous arguments and cited case law demonstrating a lack of inherency in the cited art. Applicants assert that to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference. *In re Robertson,* 169 F.3d 743, 745 (Fed. Cir. 1999).

Applicants further state that the fact that a certain result or characteristic may be present in the prior art is not sufficient to establish the inherency -- inherency may not be established by probabilities or possibilities. *Continental Can Co. USA, Inc., v. Monsanto Co., 948 F.2d 1264, 1268* (Fed Cir. 1991); *In re Rijckaert,* 9 F.3d 1531, 1534 (Fed. Cir. 1993). Applicants argue that it is not sufficient that a person following the teachings of the cited art sometimes obtains the claimed result -- it must invariably happen. Applicants submit that the cited art does not inherently anticipate the claimed methods for the reasons already of record and further in view of the evidence submitted herewith. With regard to the obviousness double patenting rejections set forth at sections 21 and 22 of the Final Office Action, Applicants state that inherency has no place in obviousness arguments.

Applicants' arguments and the evidence have been carefully considered, but are not persuasive. As has been established in detail at paragraphs 10(III), 10(IV), 10(V), 10(VI), 10(VII) and 10(VIII) of the Examiner's answer mailed 02/13/09; at paragraphs 11, 12, 14, 15, 16 and 17 of the Office Action mailed 05/28/08; and at paragraphs 21, 22, 26, 27, 28 and 29 of the Office Action mailed 02/11/08, the prior art method necessarily includes all of the elements of the instant claims.

The extrinsic evidence does make clear that the missing descriptive matter is necessarily present in the thing described in the applied references and therefore establishes inherency. As set forth previously, that the determination of inherency in the instant case is not established by probabilities or possibilities is evidenced by the teachings of Thompson *et al.* (*Diabetes* 46: Suppl. 1, page 30A, 0116, 02 May 1997, of record) (Thompson

et al. May, 1997). The reference of Thompson *et al*. establishes that the missing inherent matter is necessarily present in the method thing described in the prior art reference. Thompson *et al*. (May, 1997) showed that a method of subcutaneous administration of pramlintide, i.e., $^{25, 28, 29}$pro-h-amylin, an analog of human amylin, i.e., the same amylin agonist used in the instant invention, to patients with type II diabetes requiring insulin, at a dose 60 micrograms QID (i.e., four times a day) or TID (i.e., three times a day) not only improved glycemic control in these patients, ***but also decreased body weight*** concurrently (see abstract) and therefore necessarily served as a method of treating obesity. It is important to note that the *human patients used in the instant specification for treatment of obesity via administration of pramlintide are indeed type II diabetic human patients*. As set forth previously, the prior art disclosure is commensurate in scope with the instant disclosure with regard to the type 2 diabetic human subject population used, the pramlintide compound administered, the amount and frequency of pramlintide administered, to the type 2 diabetic human patients. The same two methods (i.e., the prior art method and the instant method) cannot have mutually exclusive results. Applicants' Exhibit I clearly shows that a significant number (about 47%) of the diabetic patient species did not gain weight or *lost weight* with the pramlintide treatment and therefore met the definition of the limitation 'treating obesity' in the last paragraph of the instant specification, i.e., 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'.

Similarly, that the determination of inherency in the instant case with regard to the method of Kolterman (1996) is certainly not established by probabilities or possibilities is further evidenced by the teachings of Ratner *et al*. (*Exp. Clin. Endocrinol. Diabetes* 113: 199-204, 2005, of record) (Ratner *et al*. 2005). The reference of Ratner *et al*. (2005), which is co-authored by the inventor OG Kolterman, show that subcutaneous administration of 30 or 60 micrograms of TID or QID pramlintide to insulin-taking IDDM patients having a body weight of 76.0 $\pm$ 14.3 kg or a BMI of > 25 kg/m^2, concurrently induced *a significant decline in weight*. See sections 'Subjects and Methods'; Results; Table 1; and Figure 1B of Ratner *et al*. (2005). Therefore, Kolterman's (1996) method necessarily served as a method of treating obesity. It is particularly noted that Applicants have advanced no arguments with regard to the teachings of Ratner *et al*. (2005), the reference that was cited to show that the missing inherent matter is necessarily present in the method thing described in the prior art reference of Kolterman *et al*. (1996).

As set forth previously, an anticipatory reference has to teach only one species or one embodiment encompassed by the scope of the genus claims. Under the principles of inherency, a reference may be directed to an entirely different problem than the one addressed by the inventor, or may be from an entirely different field of endeavor than that of the claimed invention, yet the reference is still anticipatory if it explicitly or inherently discloses every limitation recited in the claims. See *State Contracting & Eng'g Corp. v. Condotte America, Inc*., 346 F.3d 1057, 1068, 68 USPQ2d 1481, 1488 (Fed. Cir. 2003). Applicants appear to be arguing that in order to be anticipatory, a prior art reference has to teach each and every species or embodiment

encompassed within the scope of the instant claims. The argument is not persuasive.

The evidence of record in the instant case establishes that obesity was known to be associated and/or interrelated with type 2 diabetes mellitus in humans. Tsanev expressly taught that obesity and diabetes mellitus could not be considered in isolation since they are interrelated. See page 3 of the translated Tsanev's document. Consistent with Tsanev's teachings, Olefsky JM (*In*: *Harrison's Principles of Internal Medicine*, 12th Edition, McGraw-Hill Book Company, pages 411-416, 1961, of record) documented as early as in 1961 that the type of diabetes wherein 80 to 90% are 'obese' is type II diabetes. See the first full paragraph on page 414 of Olefsky JM. The applied prior art references taught the administration of pramlintide to human type II diabetes mellitus patients as explained *supra*. The extrinsic evidence from Thompson establishes that the prior art method necessarily results in weight loss in this patient population. Applicants have not identified any manipulative difference between the prior art method and the claimed method. As discussed above, the claimed method is inherent and in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art" (*Perricone,* 432 F.3d at 1377), regardless of whether the inherent result is recognized. "It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." *In re Woodruff,* 919 F.2d *1575,* 1578 (Fed. Cir. 1990). When "a claimed new benefit or characteristic of an invention otherwise in the prior art" is an inherent property of the old invention, "the new realization alone does not render the old invention patentable." *Perricone v. Medicis Pharm. Corp.,* 432 F.3d 1368, 1377 (Fed. Cir. 2005).

"[A] limitation or the entire invention is inherent and in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art." *Id.* (citations omitted). As summarized in *Perricone, id.* at 1375-76: A single prior art reference that discloses, either expressly or inherently, each limitation of a claim invalidates that claim by anticipation. *Minn. Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.,* 976 F.2d *1559, 1565* (Fed. Cir. 1992). Thus, a prior art reference without express reference to a claim limitation may nonetheless anticipate by inherency. *See In re Cruciferous Sprout Litig.,* 301 F.3d 1343, 1349 (Fed. Cir. 2002). "Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claims limitations, it anticipates." *Id.* (quoting *MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365 (Fed. Cir. 1999). Moreover, "[I]nherency is not necessarily coterminous with knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art." *Id.; see also Schering Corp. v. Geneva Pharms.,* 339 F.3d 1373, 1377 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition in the prior art) (citing *In re Cruciferous Sprout Litig.,* 301 F.3d at 1351; *MEHL/Biophile,* 192 F.3d at 1366). "Thus, when considering a prior art method, the anticipation doctrine examines the natural and inherent results in that method without regard to the full recognition of those benefits or characteristics within the art field at the time of the prior art disclosure." *Id.* at 1378. See *Ex parte Satoshi Matsubara,* decided 02/10/2010, from Appeal 2009-006581. The rejections stand.

Furthermore, contrary to Applicants' argument that inherency has no place in obviousness arguments, the inherent teaching of a prior art reference

can indeed be the basis of an obviousness rejection. In this regard, MPEP 2112 states as follows:

> The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995).

See also *In re Graselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983). There is no requirement that the disclosure of a prior art reference has to be express, but it can be inherent or implicit as in the instant case.

Rejection(s) Maintained

8) The rejection of claims 23, 24, 27, 29, 31-34, 37-39, 68, 72, 76, 80, 82, 84 and 95-97 made in paragraph 24 of the Office Action mailed 2/11/08 and maintained in paragraph 13 of the Advisory Action mailed 05/28/08 and paragraphs 9(A) and 10(I) of the Examiner's Answer mailed 02/13/09 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is maintained for the reasons set forth therein.

9) The rejection of claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 made in paragraph 28 of the Office Action mailed 2/11/08 and maintained in paragraph 16 of the Advisory Action mailed 05/28/08 and paragraphs 9(D) and 10(IV) of the Examiner's Answer mailed 02/13/09 under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al*. (*Diabetologia* 39: 492-499, April, 1996, of record) (Kolterman *et al*., 1996) as evidenced by Itasaka *et al*. (*Psychiatr. Clin. Neurosci*. 54: 340-341, June 2000, of record), is maintained for the reasons set forth therein.

10) The rejection of claims 33 and the dependent claims 34, 37-39, 72, 82 and 96 made in paragraph 23 of the Office Action mailed 02/11/08 and

maintained in paragraphs 9(B) and 10(II) of the Examiner's Answer mailed 02/13/09 is maintained for the reasons set forth therein and herein below.

Rejection(s) Withdrawn

11) The rejection of claims 23, 24, 33 and 34 made in paragraph 21 of the Office Action mailed 02/11/08 and maintained in paragraph 11 of the Advisory Action mailed 05/28/08 and paragraph 9(G) of the Examiner's Answer mailed 02/13/09 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al.* ('411, of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, English abstract, of record), is withdrawn. A new modified rejection is set forth below. The rebuttal provided in paragraph 10(VI) of the Examiner's Answer mailed 02/13/09 is still applicable.

12) The rejection of claims 23 and 33 made in paragraph 22 of the Office Action mailed 2/11/08 and maintained in paragraph 12 of the Advisory Action mailed 05/28/08 and paragraph 9(H) of the Examiner's Answer mailed 02/13/09 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, English abstract, of record) and Rink *et al.* (US 5,739,106, of record) ('106), is withdrawn. A new modified rejection is set forth below. The rebuttal provided in paragraph 10(VIII) of the Examiner's Answer mailed 02/13/09 is still applicable.

13) The rejection of claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 made in paragraph 26 of the Office Action mailed 2/11/08 and maintained in

paragraph 14 of the Advisory Action mailed 05/28/08 and paragraph 9(C) of the Examiner's Answer mailed 02/13/09 under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al*. (WO 96/40220, already of record) ('220) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, English abstract, of record), is withdrawn. A new modified rejection is set forth below. The rebuttal provided in paragraph 10(III) of the Examiner's Answer mailed 02/13/09 is still applicable.

14) The rejection of claims 23, 24, 29, 33, 34 and 38 made in paragraph 27 of the Office Action mailed 2/11/08 and maintained in paragraph 15 of the Advisory Action mailed 05/28/08 and paragraph 9(E) of the Examiner's Answer mailed 02/13/09 under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta *et al*. (US 5,686,411, of record) ('411) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, English abstract, of record), is withdrawn. A new modified rejection is set forth below. The rebuttal provided in paragraph 10(V) of the Examiner's Answer mailed 02/13/09 is still applicable.

15) The rejection of claims 23, 24, 27, 29, 33, 34, 37 and 38 made in paragraph 29 of the Office Action mailed 02/11/08 and maintained in paragraph 17 of the Advisory Action mailed 05/28/08 and paragraph 9(F) of the Examiner's Answer mailed 02/13/09 under 35 U.S.C § 102(e)(2) as being anticipated by Beumont *et al*. (US 5,321,008, of record) ('008) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, English abstract, of record), is withdrawn. A new modified rejection is set forth below. The rebuttal provided in paragraph 10(VII) of the Examiner's Answer mailed 02/13/09 is still applicable.

Rejection(s) under 35 U.S.C § 102

16) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

17) Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 are rejected under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al*. (WO 96/40220, of record) ('220) as evidenced by Olefsky JM (*In*: *Harrison's Principles of Internal Medicine*, 12th Edition, McGraw-Hill Book Company, pages 411-416, 1961, of record) and/or Tsanev (*Vutr. Boles* 23: 12-17, 1984, Original, PubMed English abstract, and English translation, of record).

It is noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See last paragraph on page 12 of the specification. It is further noted that the patient population used in the instant invention to treat obesity by the administration of the recited amount of pramlintide is insulin-requiring Type 2 diabetics. See Example 1 of the instant specification.

Kolterman *et al.* ('220) taught a method of administering to insulin-taking type II diabetic human subjects a dose of 10, 30, 50, 60 or 150 micrograms per day (i.e., the amount falling in the range recited in the instant claims) of the amylin agonist composition, pramlintide or $^{25, 28, 29}$pro-h-amylin, also known as AC137, i.e., the same amylin agonist administered in Examples 1 and 3 of the instant invention. The composition consisted of pramlintide and a pharmaceutically acceptable carrier, and was administered in single or multiple doses, for example, of about 30 micrograms QID, or about 60 micrograms TID or QID, i.e., an amount effective to treat obesity. See pages 9-11; paragraph bridging pages 20 and 21; page 21; first paragraph on page 19; lines 8-10 on page 19; and the first row reciting 'Insulin-Treated Patients' in each Table of Kolterman *et al.* ('220). Pramlintide was administered subcutaneously 1-4 times a day, before meals. See pages 9 and 22. Kolterman *et al.* ('220) additionally taught that the presence of obesity is a characteristic of 'most patients with Type II diabetes mellitus'. See page 10. Kolterman *et al.* ('220) taught the benefit of obtaining weight loss in Type II diabetic patients by teaching that hyperglycemia associated with Type II diabetes can be reversed or ameliorated by *weight loss* sufficient to restore the sensitivity of the peripheral tissues to insulin (see pages 7, first paragraph), thus teaching that Type II diabetic patients are indeed in need of treatment for obesity or weight loss. Thus, the very active step of the instantly claimed method was disclosed and practiced by Kolterman *et al.* ('220) in 1996 in the very same patient population, i.e., a human type II diabetes mellitus patients used by Applicants in Example 1 of the instant application. The prior art method is the *same* as the instantly claimed method with regard to the pramlintide amylin agonist or the amylin agonist analogue,

the amylin agonist composition or the pramlintide amylin agonist analogue composition administered, and the insulin-taking Type II diabetic patients used (80-90% of Type II diabetic patients being known in the art to be intrinsically obese as taught by Olefsky JM or Tsanev - see the first full paragraph on page 414 of Olefsky JM and Tsanev's English abstract), the subcutaneous route of the administration used, the dose and the daily frequency of the amylin agonist pramlintide administered, and the administration step prior to meals. Given Tsanev's express disclosure that obesity and diabetes mellitus cannot be considered in isolation since they are interrelated (see page 3 of English translated Tsanev) and given Olefsky's and Tsanev's express disclosure that 80 to 90% of type II diabetic patients are intrinsically obese, and given Kolterman's ('220) recognition that obesity is an intrinsic characteristic of most patients with Type II diabetes mellitus and the indication that these patients are in need of weight loss, Kolterman's ('220) method of subcutaneous administration of pramlintide to Type II diabetic patients in an amount that falls within the range recited in the instant claims, necessarily serves as the claimed method of treating obesity, and therefore anticipates the instantly claimed method. Since 80-90% of Type II diabetic patients are known in the art to be intrinsically obese, 80-90% of Kolterman's ('220) type II diabetic patients to whom pramlintide composition was administered, necessarily qualify as human subjects in need of treatment of obesity as recited in the instant claims. The Office's position that Kolterman's ('220) method is the same as the Applicants' claimed method is based upon the fact that the method step, the pramlintide compound administered, the amount of the compound administered, the route by which the compound is administered, and the intrinsically obese diabetic

human patient species to which the pramlintide compound was administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of type 2 diabetic patients as disclosed by Olefsky JM or Tsanev, Kolterman's ('220) method of administration of the above-identified therapeutically effective amount (i.e., about 30 micrograms QID, or about 60 micrograms TID or QID, or a dose of 10, 30, 50, 60 or 150 micrograms per day) of the amylin agonist ^{25,28,29}Pro-human amylin to intrinsically obese type 2 diabetic human subject species anticipates the instant claims. Given that the method step of the Kolterman's ('220) method and the instant claims are the same, Kolterman's ('220) method is expected to bring about obesity-treating effect, weight gain-inhibiting or weight loss-causing therapeutic effect in the intrinsically obese pramlintide-treated type II diabetic patients. The obesity-relief, weight gain inhibition, or weight loss-induction is an inherent property inseparable from the administered pramlintide.

The evidence of record in the instant case establishes that obesity was known to be associated and/or interrelated with type 2 diabetes mellitus in humans. Tsanev expressly taught that obesity and diabetes mellitus could not be considered in isolation since they are interrelated. See page 3 of the translated Tsanev's document. Consistent with Tsanev's teachings, Olefsky JM documented as early as in 1961 that the type of diabetes wherein 80 to 90% are 'obese' is type II diabetes. See the first full paragraph on page 414 of Olefsky JM. Thus, it was known at the time of the invention that 80-90% of type II diabetic patients are intrinsically obese.

Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 are anticipated by Kolterman *et al.* ('220). The publication of Olefsky JM or Tsanev is **not** used

as a secondary reference in combination with the reference of Kolterman *et al*. (‘220), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman *et al*. (‘220), with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). ‘To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.’ *Continental Can Co. USA v. Monsanto Co*., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc*., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Olefsky’s and/or Tsanev’s extrinsic evidence makes clear that the missing descriptive matter, i.e., 80 to 90% prevalence of obesity in Kolterman’s (‘220) type II diabetic subject species administered with pramlintide, is necessarily present in the method thing described by Kolterman *et al*. (‘220). The method of Kolterman *et al*. (‘220) clearly anticipates the claimed method of the instant invention, because Kolterman *et al*. (‘220) taught the very step of the instantly claimed method in the very same human patient population species. The alleged failure of Kolterman (‘220) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Kolterman’s (‘220). Where the result is a necessary

consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc*., 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983). Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the disclosure of Kolterman *et al*. ('220), Kolterman's ('220) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect. The obesity-relief or weight loss-induction is an inherent property inseparable from the administered pramlintide. The two structurally identical pramlintide compounds administered in the two methods (i.e., the prior art method and the instant method) cannot have mutually exclusive properties. The same two methods cannot have mutually exclusive results.

18) Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 are rejected under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al*. (*Diabetologia* 39: 492-499, April, 1996, of record) (Kolterman *et al*., 1996) as evidenced by Itasaka *et al*. (*Psychiatr. Clin. Neurosci*. 54: 340-341, June 2000, of record).

It is noted that the human patient in need of the recited treatment according to the instant invention is expressly identified in the instant specification as one having a body weight of 79 kg. A 70 kg patient is *not* excluded from the scope of the instant invention 'as a human subject in need thereof', but is expressly included. The recited therapeutic amount range of 'about 0.1 milligrams per day to about 1 milligram per day', or 'about 0.01 to about 5 mg/day', or 0.03 to about 5 mg/day of the amylin agonist or amylin

agonist analogue, pramlintide, administered is specifically "for a 70 kg patient". See last paragraph of page 27 of the specification. A diabetic human patient having a baseline BMI of up to 27.0 kg/m^2 is not excluded from the scope of the instant invention 'as a human subject in need thereof', but is expressly included. See lines 25 and 26 of page 35 of the instant specification.

It is further noted that the claimed method of treating obesity in a human subject in need thereof encompasses alleviating the 'symptoms' of the disorder, i.e., obesity. See the last paragraph on page 12 of the instant specification. The substitute specification at paragraph bridging pages 10 and 11 characterizes 'increased appetite' as a sign strongly associated with obesity. Thus, increased appetite and therefore, increased food intake is viewed as a 'symptom' of obesity. It is further noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See last paragraph on page 12 of the instant specification.

Kolterman *et al.* (1996) taught a method of subcutaneous administration of 30, 100, or 300 μg of pramlintide composition or AC137 (i.e., $^{25, 28, 29}$pro-h-amylin, the same one used in Applicants' Example 2), a human amylin analogue, to human patients with insulin-dependent diabetes mellitus or IDDM who were on insulin. Pramlintide was administered three times daily for a period of 14 days. See abstract; and page 493. The mean body weight $\pm$ SEM of diabetic patients included in Kolterman's (1996) method who were administered subcutaneously with 30 micrograms, 100 micrograms, and 300 micrograms of pramlintide, three times a day for 14 days, was 70.6 $\pm$ 2.7, 74.4

± 2.5, and 75.7 ± 2.6 respectively. Therefore, the 70.6 to 75.7 kg insulin-taking diabetic patients from Kolterman's (1996) study qualify as human subjects in need of treatment for obesity as recited in the instant claims. Additionally, even BMI-wise, Kolterman's (1996) diabetic subjects meet the limitation 'a human subject …. in need of treatment for obesity' as recited in the instant claims, because the diabetic subjects included in Kolterman's method (1996) had a BMI of up to 27. See second full paragraph under 'Subjects, materials and methods'. Therefore, Kolterman's (1996) diabetic subjects having a BMI at least in the range of 24 up to 27 do qualify as diabetic subjects in need of treatment for obesity in light of what is known in the art. For example, Itasaka *et al*. teach that a BMI of 24.0 to 26.4 represents mild obesity and 26.4 and heavier (i.e., including a BMI of 26.4 to 27) represents obesity in humans. See abstract of Itasaka *et al*. Kolterman's (1996) pramlintide composition did not comprise another obesity relief agent, but consisted of pramlintide. The pramlintide composition was injected subcutaneously to the human patients (see 'Study design') and therefore is expected to inherently contain a pharmaceutically acceptable carrier therein. The amount administered was 30 micrograms or 100 micrograms three times a day, or 300 micrograms per day. See 'Study design'; Table 1; and paragraph there below. Kolterman's (1996) subcutaneous administration of a therapeutically effective amount of the amylin agonist, pramlintide, to diabetic human subject species taking insulin and weighing 70 kg or more, or having a BMI falling in the BMI range of 24 up to 27, anticipates the claims drawn to Applicants' method of treating obesity in human subject genus in need thereof, as claimed currently. Thus, the very active step recited in the instantly claimed method was disclosed and practiced by Kolterman *et al*. in April,

1996. Given that the method step in Kolterman's (1996) method and the instant claims are the *same*, and the amylin agonist analogue pramlintide administered and its amount administered are the *same*, Kolterman's (1996) method is expected to necessarily bring about the same obesity-treating, weight gain-inhibiting (i.e., maintaining of existing body weight), or weight loss-inducing therapeutic effect in Kolterman's (1996) pramlintide-treated diabetic patient species who are on insulin. Since the prior art clearly taught the claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide administered in the claimed method are merely inherent and do not necessarily make the claimed method patentable. The prior art method of administering the above-explained amount of the amylin agonist ^{25,28,29}Pro-human amylin (the same pramlintide administered in Applicants' Example 2) to insulin-taking diabetic human subject species weighing 70 kg or more, and/or having a BMI falling in the range of 24 up to 27 necessarily serves as the Applicants' method of treating obesity by inhibiting weight gain or inducing weight loss, as claimed currently.

Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 are anticipated by Kolterman *et al*. (1996). The publication of Itasaka *et al*. is **not** used as a secondary reference in combination with the reference of Kolterman *et al*. (1996), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman *et al*. (1996) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described

in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co*., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc*., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Itasaka's extrinsic evidence makes clear that the missing descriptive matter, i.e., Kolterman's (1996) insulin-taking, pramlintide-administered diabetic subject species having a BMI at least in the range of 24 up to 27 necessarily qualifying as diabetic subjects in need of treatment for obesity, is necessarily present in the method thing described by Kolterman *et al*. (1996). The method of Kolterman *et al*. (1996) clearly anticipates the claimed method of the instant invention, because Kolterman *et al*. (1996) taught the very step of the instantly claimed method in diabetic human patient species. The alleged failure of Kolterman *et al*. (1996) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Kolterman *et al*. (1996). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc*., 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983). Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the disclosure of Kolterman *et*

al. (1996), Kolterman's (1996) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect. The obesity-relief or weight loss-induction is an inherent property inseparable from the administered pramlintide. The two structurally identical pramlintide compounds administered in the two methods (i.e., the prior art method and the instant method) cannot have mutually exclusive properties. The same two methods cannot have mutually exclusive results.

19) Claims 23, 24, 29, 33, 34 and 38 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta *et al*. (US 5,686,411, of record) ('411) as evidenced by Olefsky JM (*In*: *Harrison's Principles of Internal Medicine*, 12th Edition, McGraw-Hill Book Company, pages 411-416, 1961, of record) and/or Tsanev (*Vutr. Boles* 23: 12-17, 1984, Original, PubMed English abstract, and English translation, of record).

The limitation 'method … comprising ….. wherein said compound is not administered in conjunction with another obesity relief agent' in claim 23, and the limitation 'composition comprising an obesity relief agent …. carrier' in claim 33 do not exclude the presence of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent, etc. in the recited composition.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Gaeta *et al*. ('411) taught a method of treatment of diabetes mellitus in a mammal, including a patient seen by a medical practitioner, i.e., a human, comprising the administration to said mammal (human) of a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (pramlintide). See claims 34, 35 and 19; and lines 45-53 in column 7 of the '411 patent. Gaeta *et al*. ('411) taught the 'therapeutically effective amount' of the amylin agonist to include the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. See lines 53-59 in column 8. The amount effective to treat obesity encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls in the range of therapeutically effective amount of the amylin agonist disclosed in the '411 patent. Lines 9-14 of column 3 of the U.S. patent '411 describe that the limitation 'diabetes mellitus' includes insulin-requiring diabetes mellitus and that the administration is of amylin agonist analogue *alone*. The amylin agonist composition comprises a pharmaceutical carrier and the amylin agonist without insulin or glucagon. See lines 9-11 in column 7 and lines 37-39 in column 8. Given Tsanev's express disclosure that obesity and diabetes mellitus cannot be considered in isolation since they are interrelated (see page 3 of English translated Tsanev) and given Olefsky's and Tsanev's express disclosure that 80 to 90% of diabetic patients are intrinsically obese, the diabetic patient administered with the amylin agonist ^{25,28,29}Pro-human amylin in the method disclosed by the '411 patent qualifies a man patient in need of treatment for obesity. Given that the method step of the '411 patent and the instant claims are the *same*, the amylin agonist, ^{25,28,29}Pro-human

amylin, administered and the amount administered are the *same*, the method of the '411 patent is expected to bring about an obesity-treating therapeutic effect, weight gain-inhibiting effect, and weight loss-inducing effect in the intrinsically obese ^{25,28,29}Pro-human amylin-treated insulin-requiring diabetic patient of Gaeta ('411) as defined in the instant invention. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the teachings of the '411 patent, Gaeta's ('411) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect. The Office's position that Gaeta's ('411) method is the same as the Applicants' claimed method is based upon the fact that the method step, the amylin agonist, ^{25,28,29}Pro-human amylin administered, the amount of the ^{25,28,29}Pro-human amylin administered, and the intrinsically obese diabetic human patient species to whom the ^{25,28,29}Pro-human amylin is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev or Olefsky JM, Gaeta's ('411) method of administration of the above-identified therapeutically effective amount (i.e., 0.1 to 5 mg, or 0.5 to 1.0 mg) of the amylin agonist ^{25,28,29}Pro-human amylin to intrinsically obese insulin-requiring diabetic human subject species anticipates the instant claims. Given that the method step of the Gaeta's ('411) method and the instant claims are the *same*, Gaeta's ('411) method is expected to bring about the obesity-treating effect, weight gain-inhibiting, or weight loss-causing effect, against the intrinsic obesity in the ^{25,28,29}Pro-human amylin-treated, insulin-requiring human diabetic patient species. The obesity-relief, weight gain inhibition, or weight

loss-induction is an inherent property inseparable from the administered pramlintide. Since the prior art clearly taught the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist ^{25,28,29}Pro-human amylin in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

The evidence of record in the instant case establishes that obesity was known to be associated and/or interrelated with diabetes mellitus in humans. Tsanev expressly taught that obesity and diabetes mellitus could not be considered in isolation since they are interrelated. See page 3 of the translated Tsanev's document. Consistent with Tsanev's teachings, Olefsky JM documented as early as in 1961 that 80 to 90% diabetics are 'obese'. See the first full paragraph on page 414 of Olefsky JM. Thus, it was known at the time of the invention that 80-90% of type II diabetic patients are intrinsically obese.

Claims 23, 24, 29, 33, 34 and 38 are anticipated by Gaeta *et al*. ('411). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Gaeta *et al*. ('411), but rather is used to show that every element of the claimed subject matter is disclosed by Gaeta *et al*. ('411) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co*., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that

as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's and/or Olefsky's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in Gaeta's ('411) insulin-requiring diabetic subjects administered with ^{25,28,29}Pro-human amylin, is necessarily present in the thing described by Gaeta *et al.* ('411). The method of Gaeta *et al.* ('411) clearly anticipates the claimed method of the instant invention, because Gaeta *et al.* ('411) taught the very step of the instantly claimed method in the very same diabetic human patient species. The alleged failure of Gaeta *et al.* ('411) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Gaeta *et al.* ('411). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

20) Claims 23, 24, 27, 29, 33, 34, 37 and 38 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Beumont *et al.* (US 5,321,008, of record) ('008) as evidenced by Olefsky JM (*In*: *Harrison's Principles of Internal Medicine*, 12th Edition, McGraw-Hill Book Company, pages 411-416, 1961, of record) and/or Tsanev (*Vutr. Boles* 23: 12-17, 1984, Original, PubMed English abstract, and English translation, of record).

It is noted that the limitation 'method … comprising ….. wherein said compound is not administered in conjunction with another obesity relief agent' in claim 23, and the limitation 'composition comprising an obesity relief agent …. carrier' in claim 33 do not exclude the presence of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent, etc. in the recited composition. It is further noted that 'amylin agonist' is defined in the instant specification as a peptide or non-peptide compound that mimics the effect of amylin. See third paragraph of the specification under 'Summary of the Invention'. Calcitonin and CGRP are described in the instant specification as sharing the food intake-suppressing action or effect of peripherally or centrally administered amylin. See first full paragraph on page 9 of the instant specification.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Beumont *et al*. ('008) taught a method of subcutaneous administration to an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus a therapeutically effective amount of an amylin agonist *alone* such as calcitonin, or calcitonin and insulin, contained in a pharmaceutically acceptable carrier. See claims 11, 7, 13 and 4; lines 14-17 in column 5; lines 8-11 and 49-54 in column 12; and lines 34 and 35 in column 2. Claim 11 of the '008 patent is directed to the method of administering a therapeutically

effective amount of the amylin agonist calcitonin to an insulin-requiring human with diabetes mellitus. The 'therapeutically effective amount' taught by Beumont *et al*. ('008) includes the typical dosage units of about 0.1 to 1 mg of calcitonin. See first full paragraph in column 13. The amount effective to treat obesity, the amount effective to inhibit weight gain, or the amount effective to induce weight loss encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of the therapeutically effective amount disclosed in the '008 patent. Given Tsanev's express disclosure that obesity and diabetes mellitus cannot be considered in isolation since they are interrelated (see page 3 of English translated Tsanev) and given Olefsky's and Tsanev's express disclosure that 80 to 90% of diabetic patients are intrinsically obese, the diabetic patient administered with the amylin agonist ^{25,28,29}Pro-human amylin in the method disclosed by the '008 patent qualifies a human patient in need of treatment for obesity. Therefore, the method of the '008 patent comprising the administration of about 0.1 to 1 mg of calcitonin to a diabetic human species anticipates the instant claims. Given that the method step of the '008 patent and the instant claims is the *same*, and the amylin agonist administered and the amount administered are the *same* as the ones described in the instant specification, the method of the '008 patent is expected to bring about an obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect in Beumont's intrinsically obese calcitonin-treated diabetic patient as defined in the instant invention. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met

by the teachings of the '008 patent, Beumont's ('008) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain inhibiting effect, or weight loss-inducing effect. The Office's position that Beumont's ('008) method is the same as the Applicants' claimed method is based upon the fact that the method step, the amylin agonist calcitonin administered and its amount administered, the subcutaneous route by which the amylin agonist is administered, and the intrinsically obese diabetic human patient species to which the amylin agonist is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Olefsky or Tsanev, Beumont's ('008) method of administration of the above-identified therapeutically effective amount (i.e., dosage units of about 0.1 to 1 mg) of the amylin agonist calcitonin to the intrinsically obese type 2 diabetic human subject species anticipates the instant claims. Since the prior art clearly taught the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist calcitonin in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 23, 24, 27, 29, 33, 34, 37 and 38 are anticipated by Beumont *et al*. ('008). The publication of Tsanev or Olefsky is **not** used as a secondary reference in combination with the reference of Beumont *et al*. ('008), but rather is used to show that every element of the claimed subject matter is disclosed by Beumont *et al*. ('008) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to

extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co*., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc*., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in Beumont's insulin-requiring diabetic subject species administered with calcitonin, is necessarily present in the thing described by Beumont *et al*. ('008). The method of Beumont *et al*. ('008) clearly anticipates the claimed method of the instant invention, because Beumont *et al*. ('008) taught the very step of the instantly claimed method in the very same diabetic human patient species. The alleged failure of Beumont *et al*. ('008) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Beumont *et al*. ('008). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc*., 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

Double Patenting Rejections

21) The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R 3.73(b).

22) Claims 23, 24, 33 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al*. ('411, of record) as evidenced by Olefsky JM (*In*: *Harrison's Principles of Internal Medicine*, 12th Edition, McGraw-Hill Book Company, pages 411-416, 1961, of record) and/or Tsanev (*Vutr. Boles* 23: 12-17, 1984, Original, PubMed English abstract, and English translation, of record).

The method of treatment claimed in claims 34 and 35 of the '411 patent includes administering to a mammal with diabetes mellitus a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (pramlintide). The portion of the disclosure of the '411 patent at lines 45-53 in column 7 supporting the limitation 'mammal' does not exclude, but expressly includes a patient seen by a medical practitioner, i.e., a human. The portion of the disclosure of the '411 patent at second paragraph under 'Summary of the Invention' supporting the limitations 'diabetes mellitus' and 'administration of …. an amylin agonist analogue' include *insulin-requiring* diabetes mellitus and administration of an amylin agonist analogue alone (i.e., consisting of) or in conjunction with insulin or a glucagon, i.e., not in conjunction with another obesity relief agent. The portion of the disclosure of the '411 patent at lines 53-59 in column 8 supporting the limitation 'therapeutically effective amount' of the amylin agonist includes the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. The amount effective to treat obesity, encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day, or 300 micrograms per dose, falls within the range disclosed in the '411 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of the *insulin-requiring* diabetic patients as disclosed by Tsanev or Olefsky, 80% to 90% of the human diabetic patient species used in the method disclosed in the '411 patent qualify as human patients in need of treatment for obesity. Therefore, the method of the '411 patent comprising or consisting of the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist, ^{25,28,29}Pro-human amylin alone or in conjunction with insulin or glucagon, to insulin-requiring diabetic human species anticipates the instant claims. Given

that the method step of the '411 patent and the instant claims are the same, the amylin agonist analogue pramlintide used and its amount administered are the same, and the human diabetic patient species used is the same, the method of the '411 patent is expected to bring about obesity-treating effect in the intrinsically obesity diabetic patient species administered with a therapeutically effective amount of the pramlintide as claimed in the instant invention. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the disclosure of Gaeta *et al*. ('411), Gaeta's ('411) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect.

23) Claims 23 and 33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of the US patent 5,321,008 issued to Beumont *et al*. ('008, of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984) or Olefsky JM (*In*: *Harrison's Principles of Internal Medicine*, 12th Edition, McGraw-Hill Book Company, pages 411-416, 1961, of record).

The method of treatment claimed in claims 11 and 13 of the '008 patent includes administering to a human with type 2 diabetes mellitus a therapeutically effective amount of the amylin agonist, calcitonin. The portion of the disclosure of the '008 patent at lines 14-17 in column 5; lines 8-11 and 49-54 in column 12; and lines 34 and 35 in column 2 that supports the claims includes subcutaneous administration to an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus a therapeutically effective amount of an amylin agonist *alone* such as calcitonin (i.e., consisting of), or calcitonin and insulin (i.e., comprising) contained in a pharmaceutically

acceptable carrier. The portion of the disclosure of the '008 patent at first full paragraph in column 13 of the '008 patent supporting the 'therapeutically effective amount' includes the typical dosage units of about 0.1 to 1 mg of calcitonin. The amount effective to treat obesity, or the amount effective to treat obesity encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of the therapeutically effective amount disclosed in the '008 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev or Olefsky, 80 to 90% of *insulin-requiring* human diabetic patients used in the method of the '008 patent qualify as human patients in need of treatment for obesity. Therefore, the method of the '008 patent comprising or consisting of the administration of about 0.1 to 1 mg of calcitonin to insulin-requiring diabetic human species anticipates the instant claims. Given that the method step of the '008 patent and the instant claims is the same, and the amylin agonist calcitonin administered and the amount administered are the same, and the human diabetic patient species to whom calcitonin is administered is the same as the one described in the instant application, the method claimed in the '008 patent is expected to bring about an obesity-treating effect in the intrinsically obese calcitonin-treated diabetic patient species of the '008 patent. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the teachings of the '008 patent, Beumont's ('008) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic

patients as disclosed by Olefsky or Tsanev, Beumont's ('008) method of administration of the above-identified therapeutically effective amount (i.e., dosage units of about 0.1 to 1 mg) of the amylin agonist calcitonin to 80 to 90% of intrinsically obese type 2 diabetic human subject species anticipates the instant claims.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

24) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

25) Claims 80, 82 and 84 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 80, 82 and 84 are vague and indefinite in the limitation 'about', because it is unclear what precise amount or range of amounts is encompassed within the scope of this limitation. The limitation 'about' is a relative term, is not specifically defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the claim. Is an amount of 30 $\pm$ 10, or 300 $\pm$ 20, or 30 $\pm$ 30 encompassed within the scope of the limitation 'about'?

Remarks

26) Claims 23, 24, 27, 29, 31-34, 37-39, 68, 72, 76, 80, 84 and 95-97 stand rejected.

27) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of

amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

28) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

29) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Larry Helms, can be reached on (571) 272-0832.

/S. Devi/
Primary Examiner
AU 1645

August, 2010